CHEMICAL ANALYSIS CHALLENGES IN PHARMACEUTICAL CHEMISTRY AND UNDERGRADUATE PHYSICAL CHEMISTRY LABORATORY PROJECTS USING ROTATIONAL SPECTROSCOPY

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The rotational spectroscopy research group at the University of Virginia (UVa) is also tasked with administering the year-long undergraduate physical chemistry laboratory course. The course includes an introduction to quantum chemistry, experiments in molecular spectroscopy (NMR, rotational, vibrational, and electronic) and, in the spring, a capstone miniature research project. Over the past few years, molecular rotational spectroscopy using the research instruments at UVa has been extensively incorporated into the course. The spectroscopy measurements have been motivated by challenging chemical analysis problems in pharmaceutical chemistry and attempt to connect to current research topics in physical and analytical chemistry. Two laboratory projects from the past year will be described. In the fall semester, the lab considered the problem of correctly identifying diastereomers in molecules with multiple chiral centers. The project requires combining quantum chemistry calculations with spectral analysis. The project introduces the students into the broader theme of how quantum chemistry and artificial intelligence approaches are changing the way that spectra are analyzed. In the diastereomer analysis problem, a large focus is on the revolution in structure assignment by NMR spectroscopy that has occurred as that field has coupled quantum chemistry modeling of 1H and 13C NMR spectra with Bayesian statistical analysis. A spring miniature research project focuses on the recent interest in creating selectively deuterated active pharmaceutical ingredients that have higher efficacy and safety than their normal isotope versions. Since the ruling two years ago that deuterated versions of APIs would be awarded new patent protection, the pharmaceutical industry has started to focus on the unmet needs in chemistry required to produce high-purity, selectively deuterated drugs. One unmet need is the analysis of isotopologue and isotopomer impurities in deuterated reagents and this is a problem where rotational spectroscopy has unique chemical analysis capabilities. Students are tasked with evaluating the potential of existing methods for performing isotopic impurity testing and then perform an analysis using rotational spectroscopy on a commercial deuterated reagent for pharmaceutical chemistry.